Study #9727: *Plan B* OTC Actual Use Study
(Volumes 27-30 of sNDA 21-045)

Title:	Phase 3 Non-Comparative Case Series Study of Plan B Levonorgestrel Emergency Contraceptive Pills Provided Using a Simulated Over-The-Counter Approach
Study date:	November 5, 2001 to April 11, 2002
Report date:	September 30, 2002, updated January 30, 2003
Sponsor:	Women's Capital Corporation (The sponsorship was transferred to the Barr Research in Nov, 03)
Investigators:	Family Health International (FHI), Research Triangle Park, NC
Study sites:	Five Family Planning Clinics sites (five states in US): Planned Parenthood League of Massachusetts, Boston, MA Planned Parenthood Centers of West Michigan, Grand Rapids, MI Planned Parenthood of Houston and SE Texas, Houston, TX Planned Parenthood of Central and Northern Arizona, Phoenix, AZ Planned Parenthood of Western Washington, Seattle, WA Five pharmacy stores Longs Drugs stores (in 5 cities of WA)
Study Design:	Open-label, one-arm, uncontrolled multi-center clinical trial
GCP:	Yes
Study Drug:	Plan B (0.75-mg Levonorgestrel tablet); Lot #: W110004

STUDY OBJECTIVES

Primary Objective:

To estimate the frequency of contraindicated and incorrect use of Plan B when dispensed under OTC-like conditions.

Secondary Objective:

To estimate repeat use, pregnancy, and adverse events when Plan B is dispensed under OTC-like conditions.

Additional Observation

To collect and compare uses of emergency and regular contraception at enrollment and follow-up.

METHODS

Study Procedure (Table 1)

1. Investigators used a written script to inform women presenting to the study sites about the study. Each woman who expressed an interest in study participation reviewed the Plan B label and then completed a Screening Form..

2. Eligible subjects who wished to purchase Plan B were asked to sign the Informed Consent Form, and then to complete a Background Questionnaire.

3. Each subject could purchase only one package of Plan B at a time. To purchase more, women had to repeat the enrollment process. Each woman received a Study Data Card (with stamped/addressed envelope) to complete after using Plan B and then to mail to the study site. Study staff did not provide instructions on how to use Plan B (other than the package label) unless the subject specifically asked a question; the questions and answers were recorded on a data form.

4. Subjects who purchased Plan B were contacted one week and four weeks later either by telephone or were seen in person at the study site, questioned about Plan B use, adverse events and pregnancy status. Information about prior and concomitant medications was collected but not interrupted (no restriction and no special instruction). Subjects with an uncertain pregnancy status or with adverse events (Aes) received weekly follow-up until the issue was resolved.

5. Subjects were told about monetary compensation for study participation after completing the Screening Form. They received $40 (for the clinic sites) or $45 (the pharmacy sites) compensation after both contacts.

Table 1. **Schedule of Study Procedures**

Procedure	**Screening**	**Week 1 (5-8 days)**	**Week 4 (28 days or later**	**Weekly thereafter (if necessary)**
Collect baseline and background data	X			
Determine eligibility	X			
Informed consent	X			
Provision of Plan B if eligible	X			
Provision of *Study Data Card*	X			
Collect information on use of product		X	X	
Collect information on adverse events		X	X	X
Collect information on pregnancy		X	X	X

Investigators

Family Health International (FHI) designed the study, distributed Plan B, and monitored the sites. They made at least 2 site visits during the study to monitor the progress of study, to confirm that the sites were following the protocol, and to review the data. Study staffs were trained separately at each site according to a standardized training curriculum.

Plan B Dispensing

Each subject enrolled in the study was initially allowed to purchase only one package of Plan B containing two 0.75-mg levonorgestrel tablets (a single bath with lot #W110004). The package design was the same as the approved Rx package but printed with the proposed OTC labeling (Figure 1). No patient package insert was provided with the study product.

Subjects were allowed to continue their routine medication. Information was collected about medication used in the week before enrollment and concomitantly during the study. Subjects could repeat the enrollment process at a later time to qualify to purchase more Plan B.

Subject Screening and Enrollment

Admission criteria: A woman who met the following 5 criteria was eligible to receive Plan B:

1. Requested emergency contraception for personal use.
2. Had not previously participated in the Plan B Label Comprehension study.
3. Could read English, according to her own judgment.
4. Was willing to complete questionnaires and to be contacted or return to the study site in one week and four weeks for follow-up.
5. Wanted the study product after reading the text on the outside of the study package label.

The subjects were allowed to enroll repeatedly while the study sites were open. The same subject number was used for the "re-enrolled" subjects. Supportive documents included informed consent and contact information at the admission re-visits. The intervals between uses were recorded, but the data were not statistically analyzed due to low number of repeated users.

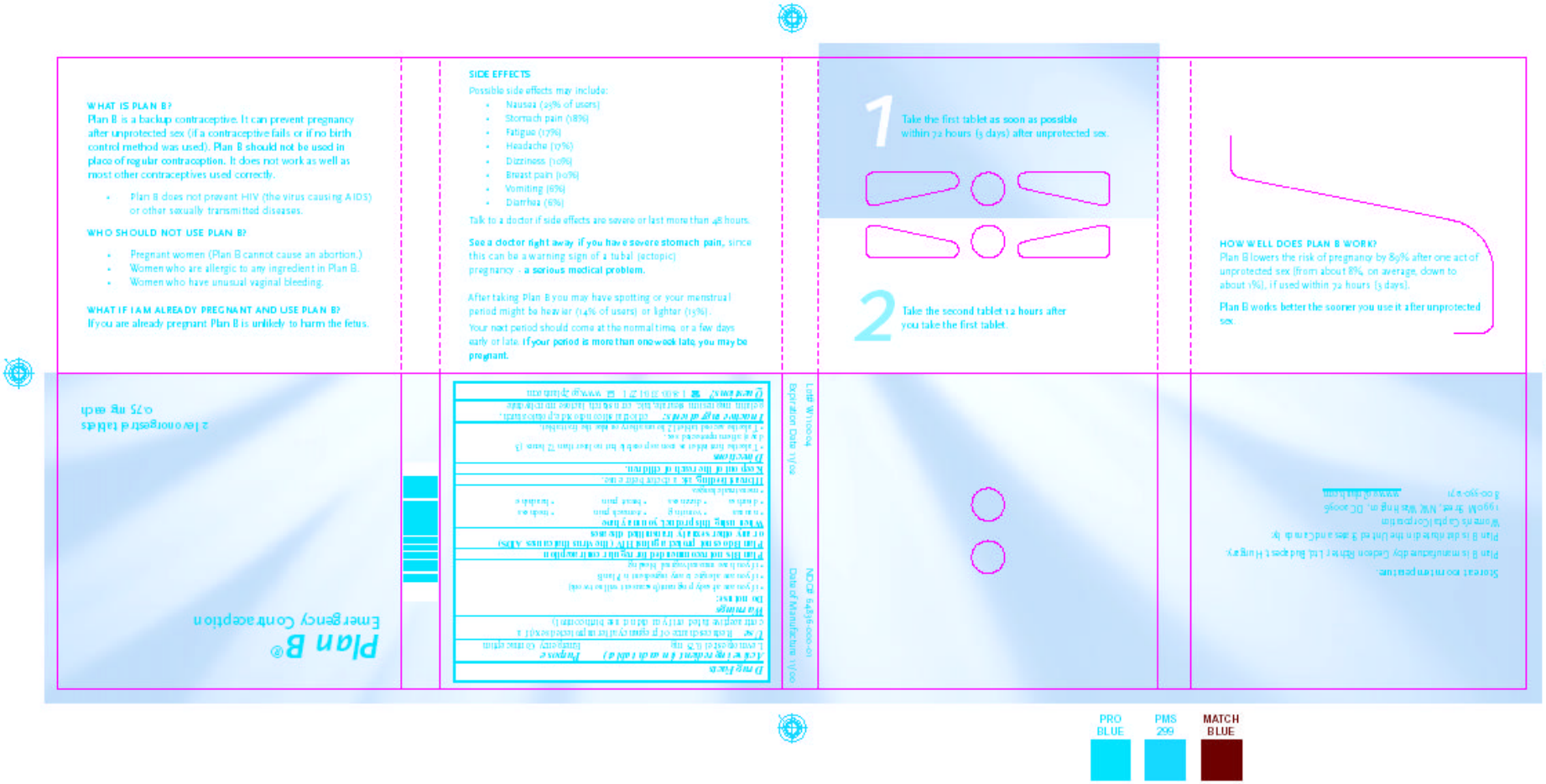

Figure 1. **Plan B Label used in the Actual Used Study**

Minor subjects: Subjects aged 15 or younger were excluded from 2 sites (Phoenix and Houston) because parental consent for this age was required. The other clinical sites did not impose age restrictions. No specific measures were taken to recruit minors at the sites so that the population would be representative of that seeking emergency contraception.

Assessment of Self-Selection/De-Selection

Self-selection: Subjects were asked to review the drug package, to complete the Screening Form and to determine whether or not the product was appropriate for them. The validity of the self-selection decision was determined based on the reasons that the subject requested and used Plan B.

Self-deselection: Contraindicated uses were evaluated for assessment of self-deselection, as follows:

Determination of Pre-existing pregnancy: Pre-existing pregnancy was evaluated at screening time (last menstrual period and usual menstrual cycle length), at follow-up contact (menstrual profile, pregnancy test results since last menstrual period (LMP), other reasons to suspect pregnancy), and by estimated fertilization date (pregnancy at least 14 days after fertilization)

Unexplained vaginal bleeding: At the earliest follow-up contact, the medical monitor determined the onset of "any unusual" vaginal bleeding, and how it was unusual, before subject took the first pill.

Allergic to the product: Information on allergy to all medications, foods and Plan B was collected during both follow-up contacts to avoid influencing behavior.

The reasons to deselect Plan B in those subjects who did not request or who received Plan B but did not use it were not evaluated in the study.

Assessment of Correct/Incorrect use

The date and time of coitus and subsequent ingestion of each pill were collected. The following questions were asked to collect data about intentional and unintentional incorrect use:

> Did you use Plan B according to all the instructions on the box? If no, what instruction did you not follow?
> Did you know you were not following the instructions when you took the Plan B pills or did you realize that only after you took the pills?

Primary analyses of incorrect use: the subjects did not follow the dosing schedule: "Take the first tablet as soon as possible within 3 days (72 hours) after unprotected sex; Take the second tablet 12 hours after you take the first tablet".

Secondary analyses of incorrect use: First tablet up to 72 hours after intercourse and second tablet up to 16 hours after the first; First tablet up to 72 hours after intercourse and second tablet up to 6-18 hours (*the rationale for this timing was not provided in the report*) after the first; First tablet up to 120 hours after intercourse and second tablet up to 24 hours after the first.

Subjects with unclassifiable use patterns were excluded in the analyses.

Safety Assessment

Adverse events were defined as medical problems that started or worsened after Plan B use

Adverse events were recorded in the Study Data Cards and were collected during the follow-up contacts (week 1, week 4 and thereafter for some subjects), and recorded in the "Adverse Events Notes page" by study staff, reviewed and then transferred to the Adverse Events data form by the clinician. The frequency, severity (mild, moderate or severe), and seriousness, and the relevance to the drug treatment were analyzed.

Site staffs did not investigate discrepancies of AE reports between the cards and the follow-up contacts unless the cards indicated the possibility of an unusual, serious, or severe event.

Adverse events were coded in COSTART terminology. The 95% confidence limits around frequencies within body system class were calculated by the exact binomial method.

Concomitant Medications: Medications used by enrolled subjects during the week before enrollment and during the follow-up period were coded according to the WHO Anatomical Therapeutic Chemical Classification system.

Efficacy Assessment

At the follow-up contacts, information about menstrual history, pregnancy test results since LMP, and any suspected pregnancy were collected and evaluated by medical monitors.

Criteria to determine pregnancy (any of the following):

a. Did not have menses following product use
b. Had a positive pregnancy test
c. Had any other evidence of pregnancy, such as ultrasound, abortion.
d. Had no evidence ruling out pregnancy as assessed by site staff.

Estimate Fertilization Date

Pregnancy occurring before Plan B use was determined by the estimated fertilization date (based on data collected from all pregnant subjects) or date of sexual intercourse. There was no diagnostic examination (ultrasound and/or blood/urine test) to confirm the fertilization date.

Criteria to exclude pregnancy

a. Had a menstrual period after Plan B use
b. Had a negative pregnancy test at least 2 weeks after the products
c. Other information (*not specified in the report*), confirmed by medical monitor individually

Undetermined pregnancy:

Subjects who did not meet the above inclusion and exclusion criteria to determine pregnancy were classified as "undermined pregnancy" and were followed up until pregnancy status was clarified.

Sexual and Contraceptive behaviors

Information about sexual behavior and contraception methods before (one month) and after (4 weeks) Plan B use were collected using multiple questions containing the following parameters:

Had sex: Subjects had sex with or without contraception during specific interval.

Had at least one sex act without contraception: included any subject who was classified as having had sex in the specified interval but indicated that she did not use any contraception at least once.

Used a "more effective" method: oral contraceptive pills, Depo-Provera, Lunelle, vasectomy, or intrauterine device at any time during the interval.

Used a "less effective" method: other than "more effective" methods, including those who did not indicate use of any method.

Used a specific contraceptive method: included any subject who indicated that she had used that method at any time in the specified interval.

Used no condoms: included any subject classified as having had sex in the specified interval who was not classified as ever having used condoms in that interval.

Subjects' reports of abstinence ("yes" answers to "have not had sex: in the past month, since receiving Plan B, or since One Week contact") were not included in these classifications because some subjects gave contradictory responses.

Data Collection

Data were collected by the investigators using the following forms at the study sites. Data recorded on all forms received at FHI were entered into the computer with Clintrial 4.3 software; the data entry system was validated by FHI data management staff.

Plan B Study Screening Form
Plan B Study Background Questionnaire
Plan B Study Disposition Form
Plan B Study One Week Contact Form
Plan B Study Four Week Contact form
Plan B Study Data Card
Plan B Study Data Card Transcription Form
Plan B Supplemental Contact Form

Study Data Card: Information about the LMP, the sex act prompting use of the product, timing of ingestion of each tablet, and pregnancy test were collected. Information was transcribed onto Study Data Card Transcription Form during site visits by FHI.

Site staffs were instructed not to investigate discrepancies between the information obtained at the follow-up contacts and on the cards.

Data Audit: There was computer hardware problem (p029, vol. 27) during the study, which may have compromised some data entries. It was/is unclear how much of the study data were affected by this problem. FHI conducted an audit analysis, showing the error rate was 0.011-0.036% of 95% CI. The sponsor stated that this was less than the pre-defined 0.05% (audited 61,336 data points from key data fields for the primary outcomes).

Data Analyses

Statistical analyses: Data were summarized in tabular forms with SAS (version 8.0). The mean, median, minimum-maximum, and standard deviation (SD) were calculated for continuous variables and frequency tables were used for categorical data. For proportions, exact binomial 97.5% confidence intervals were calculated.
[*See statistical review for certain statistical issues*].

Definition of analysis populations:

Screened Population: All subjects screened in the study and no one was excluded.

Enrolled Population: All subjects who enrolled in this study (i.e., received study product).

Per-Protocol Population: The Enrolled Population excluding subjects enrolled with violations of any of the study admission protocol criteria.

*Incomplete Follow-up Population**:*** All subjects who did not complete follow-up procedures (i.e., did not complete both scheduled contacts and all required supplemental contacts or did not mail in the Study Data Card).

Lost to Follow-up Population: All subjects who provided no follow-up data.

Missing Data: Analyses of contraindication use, incorrect use, and pregnancy included only subjects with sufficient data to allow classification of the status of the outcome. The sponsor assumed that subjects with missing data had the same outcomes as subjects who provided data.

Data obtained at visits that were outside the "per protocol" time windows were included in the primary outcome analysis. In all analyses, the data from the Study Data Cards were used only if the corresponding data from the contact visits were missing (except where otherwise noted).

Deviations from the Study Protocol

1. Informed Consents: Two versions of the Informed Consent forms were used, one (amendment #1) at 4 clinical sites and pharmacy sites and another at the Boston site (using the final version, amendment #2), as listed in Table 2. The IRB at each site approved the consent form that the site actually used. (*Reviewer: the discrepancies were minor and may not affect either subject welfare or the integrity of the data*).

2. Missing package: Study drug packages (dispensed or returned) were accounted for all sites except at the Houston site where 2 packages were missing.

3. Evaluable population: In the protocol, this was all screened subjects who met all eligibility criteria, who used the product, and who completed both follow-up contacts. In the actual analysis, the evaluable population included those subjects who received and used the study product and completed one or both follow-up contacts.

4. Repeat users: The number of repeat uses was low and thus no separate analysis was conducted in the report.

5. An analysis of "deliberate incorrect and contraindicated uses" was proposed in the protocol, but the final report focused on "unintentional incorrect and contraindicated use".

Table 2. **Differences between the informed consents used in different study sites**

Deviations	Boston Site	All others
Version of Consent Form used	Amendment #2 (final)	Amendment #1
Consult health care professionals	"Please let us know if you would like to speak with a pharmacist/clinician at any time during the research study."	"You may speak with a pharmacist/clinician at any time during the research study."
Ask additional contact	verbally inform each subject at the four-week contact (at all sites)	Grand Rapids, Seattle, and the pharmacies, but others, did not specifically state that subjects might have additional contacts after the one-month contact.
State special warning	No special warnings were used in the informed consent.	"Make sure that you understand the risks and side effects of the package insert instructions before you take the pill. If you have any questions, call [name] or the clinic/pharmacy".

RESULTS

Subject

Enrollment: A total of 665 women were screened at least once in the 5 clinical sites and 5 pharmacy sites; 585 (***88%***) subjects met all eligibility criteria and 80 **(12%)** were ineligible. The distribution of screened subjects and their eligibility were summarized in Table 3. Of the 80 ineligible subjects, 38 women who indicated eligibility did not sign the informed consent and thus became ineligible; the other 42 failed to meet one or more criteria listed in Table 4.

Table 3. **Subjects Screened and Enrolled in Each Study Site**

	Clinical Site						Pharmacy Sites	Total
	Boston	Grand Rapid	Houston	Phoenix	Seattle	Total		
Screened Subjects	129	125	170	123	79	626	39	665
Eligible Subjects	111	117	138	111	72	549	36	585
	86.0%	93.6%	81.2%	90.2%	91.1%	87.7%	92.3%	88.0%
Ineligible Subjects	18	8	32	12	7	77	3	80
	14.0%	6.4%	18.8%	9.8%	8.9%	12.3%	7.7%	12.0%

Table 4. **Reasons that screened subjects did not receive Plan B**

	Clinical Sites N=626	Pharmacy Sites N=39	Total N=665
Ineligible subjects	77	3	80
Did not sign the consent form (but eligible)	ND	ND	38
Did not think they should receive Plan B	42	0	42
Change mind	2	0	2
Indication	10	0	10
Instruction	1	0	1
Side effect	7	0	7
Want more info	17	0	17
Other options	1	0	1
No reason recorded	4	0	4

Data were extracted from text and Table 1.3 (vol. 28, p011). ND: no data available.

Subject Disposition: The disposition of subjects is summarized in Figure 2 and Table 5. Of the 585 eligible subjects, 576 (98%) were enrolled at first screening into the study (received the study product). Nine eligible subjects declined to participate in the study but 6 of them ultimately received prescription Plan B. Of the 80 ineligible subjects, 60 received prescription Plan B, 9 received the study product, 9 received no treatment and 2 received oral contraceptive pills.

Table 5. **Subjects Who Received Treatment**

Eligibility	Subjects Screened	Subjects Received Study Plan B	Subjects Received Rx Plan B	Subjects not Received Plan B
Eligible	585	576	6	3
Ineligible	80	9	60	11
Total	665	585	66	14

Demographics: The demographic characteristics of screened and enrolled populations are summarized in Tables 6 and 7. The mean age of the enrolled subjects was 22.1±5.0 (14-44) years old. Seventy-four percent of subjects were 17-25 years old and 5% were ages 14-16. Approximately 74% of the enrolled subjects had at least some college education and 0.3% had less than a 9^{th} grade education.

The demographic characteristics between the screened and enrolled populations (Table 6), and between the incomplete follow-up/lost to follow-up populations and the screened population seemed to be comparable.

All subjects ages 14-16 were in middle school or high school. Nine percent of subjects age 17-44 had less than an 11^{th} grade education; 0.2% had less than an 8^{th} grade education and 8.6% had completed 9^{th}-11^{th} grade (Table 7).

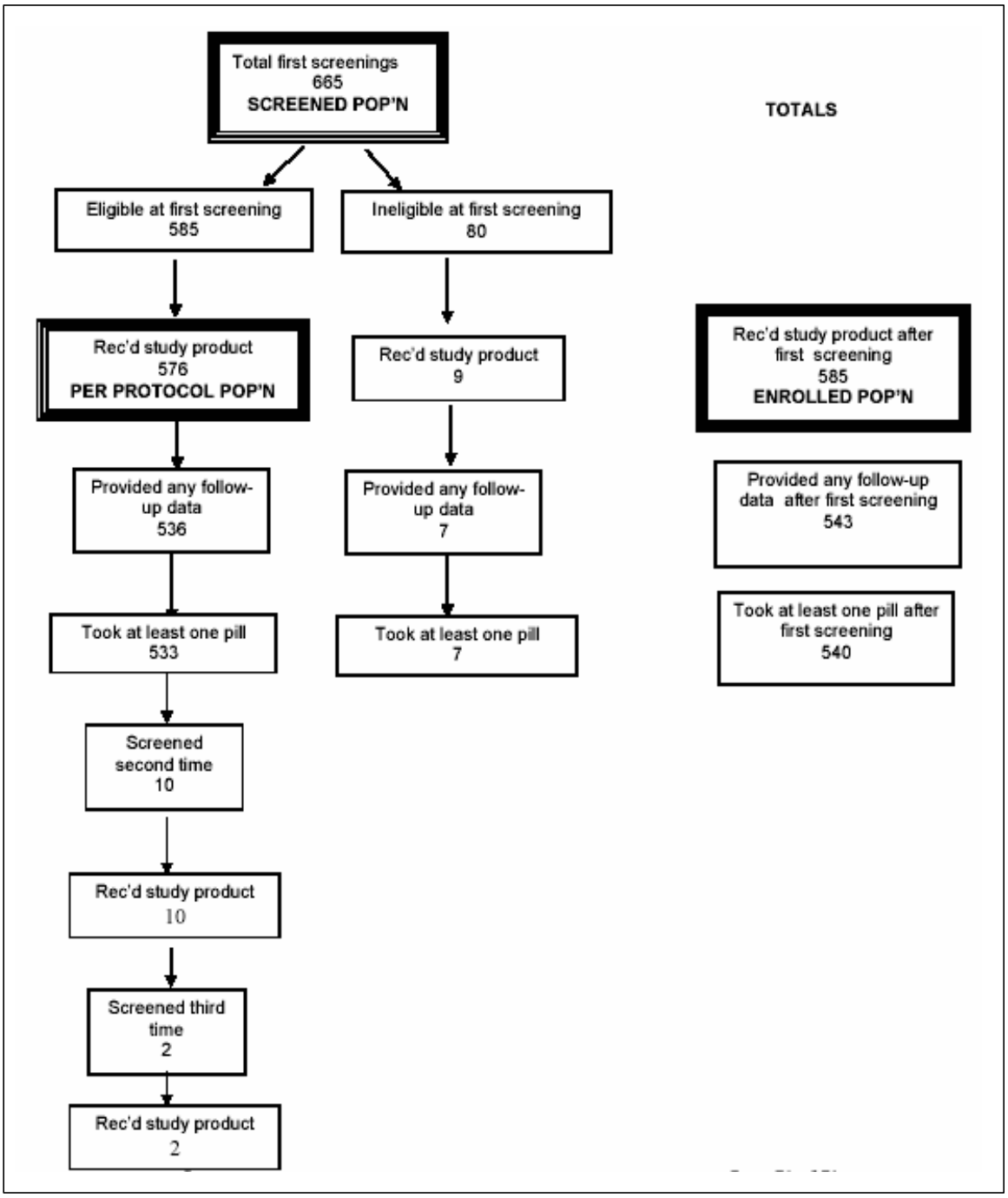

Figure 2. **Disposition of Subjects**
(Adapted from the sponsor's Figure 1 in page 070 of vol. 27)

Table 6. **Demographics of Screened and Enrolled Populations**
(Adapted from the sponsor's ***Table F*** in page 44 of vol. 27)

	Screened Population			Enrolled Population			
Age (years)	Total Clinics	Total Pharmacies	Total All Sites	Total Clinics	Total Pharmacies	Total All Sites	U.S. Women (14-44)
14-16	5.1	0.0	4.8	5.3	0	5.0	9.2
17-25	75.7	79.5	75.9	74.0	80.0	74.4	26.8
26-30	13.1	7.7	12.8	14.4	8.6	14.0	15.5
31-35	3.8	7.7	4.1	4.0	5.7	4.1	16.2
36-44	2.2	5.1	2.4	2.4	5.7	2.6	32.2
Missing	0	0	0	0	0	0	
Ethnic Hispanic							
Yes	15.0	17.9	15.2	13.8	20.0	14.2	13.9
No	84.5	79.5	84.2	85.8	77.1	85.3	86.1
Missing	0.5	2.6	0.6	0.4	2.9	0.5	
Race							
Asian	5.9	15.4	6.5	5.6	17.1	6.3	4.3
American Indian/ Alaskan Native	1.6	5.1	1.8	1.5	5.7	1.7	1.0
Black or African American	10.1	12.8	10.2	10.0	8.6	9.9	13.7
Native Hawaiian or other Pacific Islander	1.6	2.6	1.7	1.6	2.9	1.7	0.2
White	74.6	74.4	74.6	76.5	74.3	76.4	72.0
Missing	8.3	2.6	8.0	6.9	2.9	6.7	
Marital status							
Single	89.8	84.6	89.5	89.5	82.9	89.1	
Married	5.1	12.8	5.6	5.1	14.3	5.6	
Divorced	2.6	2.6	2.6	2.9	2.9	2.9	
Separated	2.2	0	2.1	2.4	0	2.2	
Missing	0.3	0	0.3	0.2	0	0.2	
Education							
8th grade or less	0.5	0	0.5	0.4	0	0.3	
9th to 11th grade	14.5	2.6	13.8	13.6	2.9	13.0	
High school/GED	13.6	20.5	14.0	12.5	22.9	13.2	
Vocational/ technical school	1.3	7.7	1.7	1.1	8.6	1.5	
Some college	48.2	48.7	48.3	49.8	45.7	49.6	
Finished college	16.1	12.8	15.9	16.4	14.3	16.2	
Graduate school	5.6	7.7	5.7	6.2	5.7	6.2	
Missing	0.2	0	0.2	0	0	0	
Household income							
$0 - 15,000	38.7	28.2	38.0	40.0	31.4	39.5	
$15,001 - 25,000	12.1	30.8	13.2	12.2	28.6	13.2	
$25,001 - 35,000	12.5	10.3	12.3	12.5	11.4	12.5	
$35,001 – 45,000	7.0	10.3	7.2	7.5	11.4	7.7	
≥ $45,001	10.7	10.3	10.7	10.7	8.6	10.6	
Missing	19.0	10.3	18.5	17.1	8.6	16.6	

Detail provided Tables 2.1.2.2a and U.S demographic data from the U.S. Census 2000.

Table 7. **Demographics of Enrolled Subjects by Age**
(% of enrolled subjects in parentheses)

Characteristics	Age (years)		Total N=585
	14-16 N=29	17-44 N=556	
Education			
= 8th Grade	1 (3.4)	1 (0.2)	2 (0.3)
9th-11th Grade	28 (96.6)	48 (8.6)	76 (13.0)
High school/Graduated	0	77 (13.8)	77 (13.2)
Vocational/Technical School	0	9 (1.6)	9 (1.5)
Some college	0	290 (52.2)	290 (49.6)
Finished college	0	95 (17.1)	95 (16.2)
Graduate School	0	36 (6.5)	36 (6.2)
Race*			
Asian	2 (6.9)	35 (6.3)	37 (6.3)
American Indian/Alaskan Native	2 (6.9)	8 (1.4)	10 (1.7)
Black	3 (10.3)	55 (9.9)	58 (9.9)
Native Hawaiian or pacific Islander	0	10 (1.8)	10 (1.7)
White	23 (79.3)	424 (79.3)	447 (76.4)
Missing	1 (3.4)	38 (6.8)	39 (6.7)
Prior EC Use			
Ever	8 (27.6)	226 (40.6)	234 (40)
Never	21 (72.4)	330 (59.4)	351 (60)

Data were extracted from Table 2.2c and g (p027 and p035 of vol. 28). * Some subject listed more than 1 race.

Compliance of Follow-up Contacts (Figure 3, Table 8)

Of the 585 enrolled subjects (576 eligible and 9 ineligible), 42 subjects (7.4%) did not provide follow-up data, constituting the Lost to Follow-up Population; 501 subjects (***85%***) completed both contacts, but only 262 subjects (45%) provided contact information within the per-protocol time windows (5-8 days for the first contact and = 28 days for the second contact). Contacts were by phone (98%) and in person (2%).

Compliance with the follow-up schedule was less complete for subjects age = 16 years and subjects with less than a high school education (Table 9). There were no significant differences in the follow-up compliance among those of different races, ethnicity and history of emergency contraceptive pill (ECP) use.

The compliance for the 1st contact was much better at the clinics than at the pharmacies.

A total 322 subjects (***55%*** of enrolled population) completed follow-up contacts (2 contacts and required supplemental contacts) and mailed the Study Data Card.

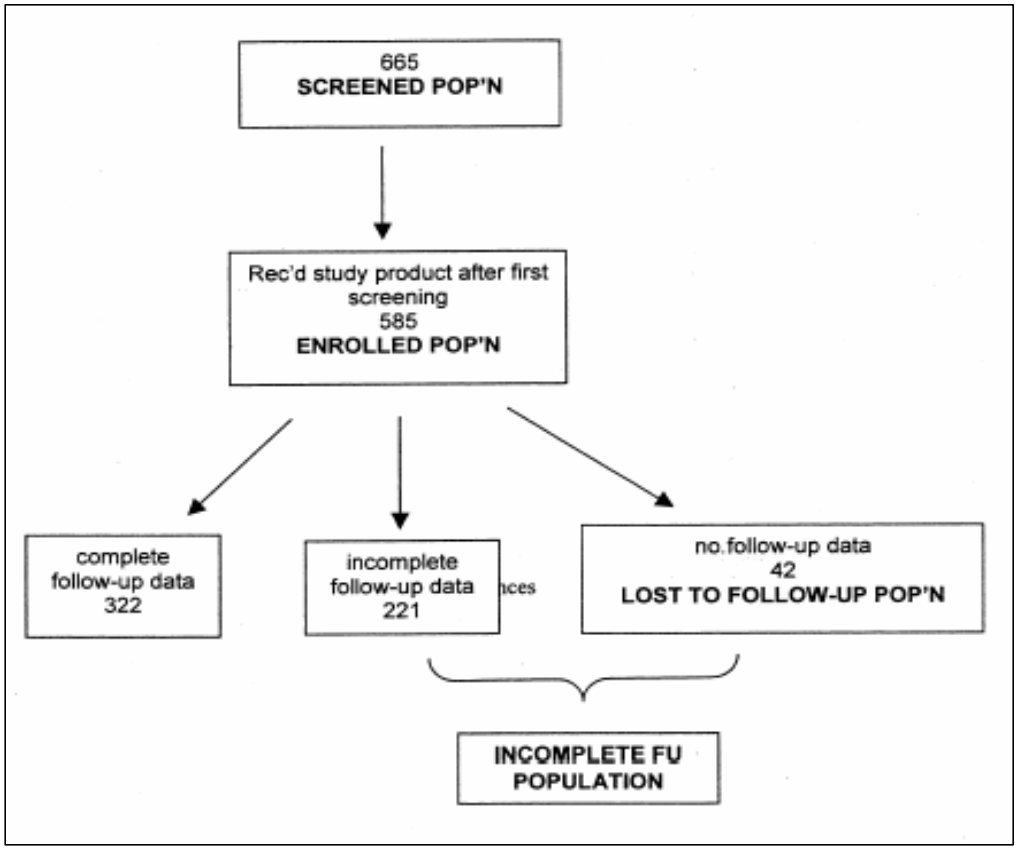

Figure 3. **Incomplete or Lost Follow-up Subjects**

The figure was adapted from the sponsor's Figure 2 in page 071 of vol. 27. "Complete follow-up" was referred to those subjects who completed = 2 follow-up contacts as well as mailed in the study data cards.

Table 8. **Compliance of Follow-up Contacts**
(% of enrolled population)

Follow-up Contact	Clinical Sites N=550	Pharmacy Sites N=35	All sites N=585
0 Contact	7.1%	11.4%	**7.4%**
1 Contact	5.3%	0	5.0%
= 2 Contacts (Total)	85.5%	88.6%	85.6%
= 2 Contacts (per protocol)†	46.5%	17.1%	**44.8%**
Timing of 1st Contact			
5-8 days	52.5%	17.1%	50.4%
Mean days (Min-Max)	11.0±7.9 (4-81)	21.3±21.6 (6-92)	11.6±9.5 (4-92)
Timing of any 2nd Contact			
= 28 days	80.7%	88.6%	81.2%
Mean Days (Min-Max)	32.5±8.0 (12-94)	38.5±14.2 (28-92)	32.9±8.6 (12-94)
Study Data Card Received	57.8%	51.4%	57.4%

Data are extracted from the sponsor's Table 1.4a (vol. 28, p012).
†The 1st contact at 5-8 days and the 2nd contact at =28 days

Table 9. **Follow-up Compliance in Subjects by Ages and Education Levels**
(% of enrolled population)

No. of Follow-up Contacts	Age (years)		Education Levels		Prior EC Use		Total N=585
	14-16	17-44	< HS	= HS	Ever	Never	
	N=29	N=556	N=78	N=507	N=234	N=351	
0	24.1	6.5	19.2	5.5	9	6.3	7.4
1	20.7	4.1	11.5	3.9	4.7	5.1	5.0
2	55.2	87.2	66.7	88.6	85.0	86.0	85.6
= 3	0	2.2	2.6	2.0	1.3	2.6	2.1

Data are extracted from Tables 1.4c and 1.4f (vol. 28, p012).

Disagreements between Follow-up Contact and the Study Data Card

Approximately **57%** of the enrolled subjects (336/585) returned the Study Data Card. Most of the returned cards (80%) contained at least one discrepancy compared to the follow-up contact. Approximately 50% of the returned cards included adverse event information that differed from the follow-up contact information; however, all AEs from the cards and the follow-up contacts were included in analysis (as seen in Safety section of this review). The overall discrepancy of data (excluding AEs) obtained from the Study Data Card was 41% (138/336) compared to the data from follow-up contacts (Table 10).

Table 10. **Discrepancies between data (excluding AEs) obtained from the Study Data Card and the Follow-up Contacts**
(% of 336 subjects who returned the Study Data Card)

Parameters	No Discrepancy	Discrepancy	Data from Card only	Data from Contact only
Onset data of menstrual period before Plan B use	61.9	33.6	1.5	3.0
Date of sex act that caused subject to want Plan B	80.1	13.1	6.3	0.6
Date and time 1st Plan B pill taken	76.5	19.0	0.9	3.6
Date and time 2nd Plan B pill taken	69.3	25.0	1.8	3.9
Had menstrual period after taking Plan B	69.3	18.8	0.3	11.6
Onset date of menstrual period after taking Plan B	73.8	19.3	1.5	5.4
Date and results of pregnancy test	81.3	3.6	3.6	11.6
All information combined	20.2	41.1	12.5	26.2

Data were extracted from Table 4.1a in page 094 of vol. 28.

Due to the low return rate of the Study Data Cards, there was greater available data from follow-up contacts for the final analyses. Considering this may have introduced interview bias into the results, the Agency sent a request to the sponsor on Oct 1, 2003 to provide data analyses based on data from the Study Card only. As per the sponsor's response on Oct 17, 2003, the incorrect use analysis using data recorded on the Study Card was no higher than that from the follow-up contact data as stratified by age, educational levels and Ever/Never EC experience.

Reproductive History

Approximately 68% of the enrolled subjects had no history of pregnancy before the first screening, and 84% had no living children (Table 11).

Table 11. **Gravidity History of Enrolled Subjects**
(% of enrolled population)

	Clinical Sites N=550	**Pharmacy Sites N=35**	**Total N=585**
Previous Pregnancy			
0	68.4	65.7	68.2
1	18.4	11.4	17.9
= 2	12.4	22.9	13.0
Missing	0.9	0.0	0.9
Living Children			
0	84.7	71.4	83.9
1	8.5	14.3	8.9
= 2	5.5	14.3	6.0
Missing	1.3	0	1.2

Data are extracted from the sponsor's Table 2.6a in page 047 of vol. 28.

Emergency Contraceptive History

About 60% of subjects had no previous experience using an emergency contraception (EC) (Tables 12 and 13). The demographic characteristics of *Ever* and *Never* EC users were comparable.

Of those with previous EC experience, 2% of subjects used it within the past month and 8% within the last 1-3 months (Table 14).

Subjects with prior emergency contraceptive use were more likely to have had at least one act of sexual intercourse without contraception in the past month ($p<0.05$) and to have a positive pregnancy history ($p< 0.01$). There were no significant differences in condom use between ever EC users and never EC users (Table 15).

Table 12. **Demographics of subjects with and without Previous Emergency Contraceptive Use Experience**
(% of the enrolled population)

Characteristics	Ever EC Use	Never EC Use	Total
	N=234 (40%)	N=351 (60%)	N=585 (100%)
Age (years)			
14-16	3.4	6.0	5.0
17-25	75.2	73.8	74.4
26-30	13.7	14.2	14.0
31-35	5.6	3.1	4.1
= 36	2.1	2.8	2.6
Education			
Some College	52.6	47.6	49.6
Finished College	13.7	17.9	16.2
High school	12.0	14.0	13.2
9^{th}-11^{th} Grade	12.0	13.7	13.0
Graduate School	8.1	4.8	6.2
Technical School	1.3	1.7	1.5
= 8^{th} Grade	0.4	0.3	0.3
Missing	0	0	0
Race*			
White	71.8	79.5	76.4
Black	13.7	7.4	9.9
Asian	5.1	7.1	6.3
Others	3.4	3.4	3.4
Missing	7.3	6.3	6.7
Marital Status			
Single	86.3	90.9	89.1
Married	7.3	4.6	5.6
Others	6.4	4.2	5.1
Missing	0	0.3	0.2

Data are extracted from the sponsor's Table 2.2g (vol. 28, p035). Some subjects had more than 1 race.

Table 13. **History of Previous Emergency Contraceptive Use**
(% of enrolled population)

	Clinical Sites	Pharmacy Site	Total
Never Used	60.7	48.6	60.0
Ever Used	39.3	51.4	40.0
(Times) 1	25.3	31.4	25.6
2	10.4	11.4	10.4
3	2.2	5.7	2.4
= 4	0.9	2.9	1.0
Missing	0.5	0	0.5

Data are extracted from the sponsor's Table 2.6a (vol. 28, p047).

Table 14. **Time since the Last Emergency Contraceptive Use**
(% of enrolled population)

Months Since Last Use	Clinical Sites N=550	Pharmacy Site N=35	Total N=585
< 1	2.2	2.9	2.2
1-3	7.8	14.3	8.2
> 3	29.3	34.3	29.6
Total	39.3	51.4	40.0

Data were extracted from the sponsor's Table H (vol. 27, p046) and Table 2.6a (vol. 28, p047).

Table 15. **Reproductive and Contraceptive History of Previous Emergency Contraceptive Users**
(% of enrolled population with or without previous ECP use)

Characteristics	Ever ECP Use	Never ECP Use	Total
	N=234 (40%)	**N=351 (60%)**	**N=585 (100%)**
Pregnancy History†			
None	62.0	72.4	68.2
1	19.7	16.8	17.9
= 2	18.4	9.4	13.0
Missing Data	0	1.4	0.9
Living Children			
None	80.3	86.3	83.9
1	10.7	7.7	8.9
= 2	9.0	4.0	6.0
Missing Data	0	2.0	1.2
Contraceptive Method			
Condoms	76.5	80.3	78.8
Withdrawal	29.9	26.8	28.0
Oral Contraceptive Pills	22.2	20.5	21.2
Spermicide	7.7	8.5	8.2
Emergency Contraception	5.6	0	2.2
Natural Family Planning	2.6	1.7	2.1
DepoProvera or Lunelle	2.6	1.1	1.7
Other	0.4	0	0.2
At least one sex act without Contraception during past month‡	65.8*	56.1	60.0

Data are extracted from the sponsor's Table 2.6g (vol. 28, p054).
† $p < 0.003$ by Kruskal-Wallis test and ‡ $p = 0.02$ by Chi-square test compared between Ever ECP and Never ECP.

History of Contraception

A total of 536 subjects (92% of the enrolled population) used a contraceptive method in the previous month (Table 16); and the most common method was the condom (79% of the enrolled population). The Lost to Follow-up population and the entire enrolled population were comparable in their histories of contraception, emergency contraception, pregnancy, and sex without contraception.

Table 16. **History of Contraceptive Methods in Previous Month**
(% of the enrolled population)

Contraceptive Method	Clinical Sites N=550	Pharmacy Sites N=35	Total N=585
Condoms	79.6	65.7	78.8
Withdrawal	29.1	11.4	28.0
Oral Contraceptive Pills	20.9	25.7	21.2
Spermicide	8.5	2.9	8.2
Emergency Contraception	2.2	2.9	2.2
Natural Family Planning	2.2	0	2.1
DepoProvera or Lunelle	1.3	8.6	1.7
Other	0.2	0	0.2
At least one sex act without contraception	60.2	57.1	60.0

Data were extracted from the sponsor's Table I (vol. 27, p046) and Table 2.6a (vol. 28, p048).

Reasons to request Plan B (Table 17): The major reasons for the 585 enrolled subjects to request Plan B during the recruitment visit were "condom broke/slipped" (37%), "unprotected sex" (33%), "prevent pregnancy" (17%), and "Oral Contraceptive Pills (OCP) problem" (4%). The sponsor stated that subjects with the reason "prevent pregnancy" did not intend to use Plan B before sexual intercourse.

Ninety-seven percent had a correct reason to request Plan B (after excluding those subjects who provided "unspecified" reasons). See Table 17.

Reasons to use Plan B (Table 18)*:* Approximately 98% of 540 subjects who used Plan B after enrollment had single (91%) or multiple sex acts (7%). The main factors to prompt the subjects to take Plan B were "condom broke/slipped", "used no contraception", and "missed OCPs". Correct self-selection calculated by exclusion of the reasons "Other" and "Doesn't remember/missing data" was 95% (514 of 540 users).

Overall, the factors prompting subjects to seek and use Plan B were similar among those of different ages, races, ethnicity, educational levels, or ever/never EC use experience (Tables 17 and 18).

Table 17. **Reasons to Request Plan B at Screening/Enrollment by Subgroups**
(% of the enrolled population)

Reason to Request Plan B	Study Sites		Eligibility		Age (year)		Education		Prior EC Use		Total N=585
	Clinics N=550	Pharmacy N=35	Ineligible N=9	Eligible N=576	= 16 N=29	= 17 N=556	< HS N=78	= HS N=507	Ever N=234	Never N=351	
Condom broke or slipped	37.1	42.9	44.4	37.3	31.0	37.8	34.6	37.9	32.5	40.7	37.4
Unprotected sex	33.3	31.4	11.1	33.5	27.6	33.5	23.1	34.7	37.6	30.2	33.2
Prevent pregnancy	17.1	14.3	11.1	17.0	27.6	16.4	28.2	15.2	18.8	15.7	16.9
OCP problem	3.8	5.7	11.1	3.8	3.4	4.0	5.1	3.7	3.8	4.0	3.9
Mistake/accident	2.4	0.0	11.1	2.1	6.9	2.0	3.8	2.0	2.1	2.3	2.2
Contraceptive failure (unspecified)	1.8	0.0	0.0	1.7	0.0	1.8	0.0	2.0	1.7	1.7	1.7
Withdrawal	1.5	0.0	11.1	1.2	0.0	1.4	2.6	1.2	0.0	2.3	1.4
Prevention, unspecified	1.3	0.0	0.0	1.2	3.4	1.1	2.6	1.0	0.9	1.4	1.2
Unspecified	1.3	0.0	0.0	1.2	0.0	1.3	0.0	1.4	1.7	0.9	1.2
Sex, unspecified	0.5	2.9	0.0	0.7	0.0	0.7	0.0	0.8	0.4	0.9	0.7
Backup to spermicide	0.2	0.0	0.0	0.2	0.0	0.2	0.0	0.2	0.4	0.0	0.2
Missed injection	0.0	2.9	0.0	0.2	0.0	0.2	0.0	0.2	0.0	0.3	0.2

Data were extracted from Tables 2.10a, b, c, f and g (p061-p069 of vol. 28). The information was collected during the screening/enrollment visits.

Table 18. **Reasons to Prompt Plan B Use after Enrollment by Subgroups**
(% of subjects who used the product)

Reason to use Plan B	Study Sites		Eligibility		Age (year)		Education		Prior EC Use		Total N=540
	Clinics N=510	Pharmacy N=30	Ineligible N=7	Eligible N=533	= 16 n=22	= 17 n=518	< HS n=64	= HS n=476	Ever N=213	Never N=327	
Reason to Prompt Plan B Use (Total Responses)	100	100	100	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Single sex act	91.6	86.7	85.7	91.4	95.5	91.1	92.2	91.2	91.1	91.4	91.3
Multiple sex acts	6.9	10.0	0.0	7.1	4.5	7.1	4.7	7.4	8.5	6.1	7.0
Other reason	0.8	3.3	14.3	0.8	0.0	1.0	1.6	0.8	0.0	1.5	0.9
Missing data	0.8	0.0	0.0	0.8	0.0	0.8	1.6	0.6	0.5	0.9	0.7
Nature of Contraception Failure (Total Responses)	98.6	100	85.7	98.9	100.0	98.6	96.9	98.9	99.5	98.2	98.7
Condom broke/slipped	44.9	50.0	42.9	45.2	54.5	44.8	46.9	45.0	39.9	48.6	45.2
Used no contraception	39.8	36.7	28.6	39.8	27.3	40.2	28.1	41.2	44.6	36.4	39.6
Missed OCPs	7.1	3.3	0.0	6.9	9.1	6.8	10.9	6.3	7.0	6.7	6.9
Withdrawal	3.7	0.0	0.0	3.6	9.1	3.3	7.8	2.9	3.8	3.4	3.5
Other	2.5	10.0	14.3	2.8	0.0	3.1	3.1	2.9	4.2	2.1	3.0
Doesn't remember/missing	0.6	0.0	0.0	0.6	0.0	0.6	0.0	0.6	0.0	0.9	0.6

Data were extracted from Table 5.2a, b, c, f and g (p106- of vol. 28). The information was collected during the follow-up contacts. OCPs: oral contraceptive pills.

Contraindicated Use: There are three contraindications listed in the Warnings section of the proposed OTC label, and subjects should have deselected this product if they had any of them. A total of 523 (97%) of 540 users provided sufficient data for evaluation of contraindications after the first screening. Seventeen subjects (3.1% of 540) had insufficient data for evaluation and were excluded from analysis. The results by age, educational level, and previous EC experience were summarized in Table 19.

Seven subjects with contraindications (1.3% of 523 users) unintentionally used Plan B. The contraindicated users were in the "eligible" group; six of them were at least age 17 and had at a high school education or greater. By including 3.1% subjects with missing data, the maximum percentage of contraindicated use would be 4.4%.

Pregnancy: One subject was already pregnant when she used Plan B.

Unexplained vaginal bleeding: Six subjects had unexplained vaginal bleeding before use: one after intercourse, one early menses, and 4 unexplained bleeding.
Allergy: No subjects were allergic to Plan B.

The sponsor stated that they did not have information on the 45 subjects (585-540) who purchased Plan B but did not use it because of contraindications.

Table 19. **Contraindicated Use of Study Product**
(% of subjects who used the product)

	Age (years)		Education		Prior ECP Use		Total
	= 16	**= 17**	**< HS**	**= HS**	**Ever**	**Never**	
Users	22	518	64	476	213	327	540
Total Contraindicated Use†							
Intentional	0	0	0	0	0	0	0
Unintentional	1 (4.5)	6 (1.2)	1.6	1.3	1.4	1.2	**7 (1.3)**
Insufficient data	3 (13.6)	14 (2.7)	9.4	2.3	2.8	3.4	3.1
Pregnancy at time of Use							
Yes	0	1 (0.2)	0	0.2	0	0.3	0.2
No	86.4	97.7	93.8	97.7	98.1	96.6	**97.2**
Insufficient data	13.6	2.1	6.3	2.1	1.9	3.1	2.6
Unexplained vaginal Bleeding							
Yes	1 (4.5)	5 (1.0)	1.6	1.1	1.4	0.9	1.1
No	21 (95.5)	511 (98.6)	96.9	98.7	98.1	98.8	**98.5**
Insufficient data	0	0.4	1.6	0.2	0.5	0.3	0.4
Allergy to Plan B							
Yes	0	0	0	0	0	0	0
No	100	99.0	96.9	99.4	99.1	99.1	**99.1**
Insufficient data	0	1.0	3.1	0.6	0.9	0.9	0.9

Data were extracted from the sponsor's Tables 5.5c, f and g in page 122-127 of vol. 28.
† "Intentional" indicates that subjects correctly recognized contraindications before use and "Unintentional" indicates that subject incorrectly recognized contraindications before use.

Correct/Incorrect Plan B Use

Of the 585 enrolled subjects 540 took 2 pills or 1 pill (only one subject). A total of 506 subjects (94% of 540 users) provided sufficient data for evaluation of correct use and the remainder were excluded from the analysis.

Two subjects took the first pill before sexual intercourse (103 hours and 12.5 hours respectively). As shown in Table 20, the first pill was taken at 34.8±21.1 hours (-103 to 175 hours) in relation to the timing of sexual intercourse and the second pill was taken 12.5±3.2 hours (0-36 hours) after the first pill.

There was similar timing of Plan B use among those of different ages, ethnicities, races, educational levels and with/without emergency contraceptive experience.

Incorrect Use Analysis as per Protocol (Tables 21a & 21b): The per-protocol analysis for correct use (to take the first pill <72 hours after sex and the 2nd pill at 12 hr after the first pill), demonstrated that the correct use rate was 67.8% (366 of 540 users) and the incorrect use was from 26% (140 of 540). The incorrect use rate was 32% in a more conservative analysis that included the 34 subjects with missing data (140+34 of 540) Most errors were related to the timing of the 2nd dose.

Of the 26% incorrect uses, 1.3% (7 subjects) were intentional and 24.6% (133 subjects) were unintentional.

A re-analysis of the data based on the 506 subjects who used Plan B and provided sufficient follow-up data (Table 21b), demonstrated that the correct and incorrect use rates were 72% (366 of 506) and 28% (140 of 506), respectively.

Therefore, overall correct and incorrect use rates would be 68-72% and 26-32%, respectively.

The correct/incorrect use rates did not demonstrate clinically significant differences among the subgroups stratified by age, educational level, and previous EC experience.

Table 20. **Disposition of Plan B in the Enrolled Population**
(% of enrolled population)

	Age (years)		**Education**		**Prior ECP Use**		**Total**
	= 16	**= 17**	**< HS**	**= HS**	**Ever**	**Never**	
Enrolled Subjects	29	556	78	507	234	351	585
Gave product away							
Yes	0	1.3	0	1.4	1.3	1.1	1.2
No	75.9	92.3	80.8	93.1	89.7	92.6	**91.5**
No data	24.1	6.5	19.2	5.5	9.0	6.3	7.4
Number of pills taken							
0	0	0.5	0	0.6	0.4	0.6	0.5
1	0	0.2	0	0.2	0	0.3	0.2
2	75.9	93.0	82.1	93.7	91.0	92.9	**92.1**
No data	24.1	6.3	17.9	5.5	8.5	6.3	7.2
The first pill taken†							
Subject (%)	65.5	88.1	71.8	89.3	88.5	86.0	**87.0**
Hours after sex act	40.2±19.2 (11.5-70)	34.6±21.2 (-103-175)	35.0±18.1 (5-70)	34.8±21.5 (-103-175)	34.1±18.7 (-12.5-88)	35.3±22.7 (-103-175)	34.8±21.1 (-103-175)
The second pill taken‡							
Subject (%)	72.4	90.3	78.2	91.1	88.9	89.7	**89.4**
Hours from the 1st pill	12.1±0.5 (11-14)	12.5±3.3 (0-36)	12.9±3.0 (11-24.5)	12.5±3.2 (0-36)	12.6±3.1 (0-36)	12.5±3.2 (0-36)	12.5±3.2 (0-36)

Data were extracted from the sponsor's Tables 5.1c, 5.1f and 5.1g in page 101-105 of vol. 28.
† including subjects who took at least one pill; subjects may take pills before sex.
‡ including subjects who took pills and the interval between pills was not negative.

Table 21a. **Incorrect Use of Plan B by Primary Definition**
(% of subjects who used the product, **including** those who provided insufficient data)

	Age (years)		**Education**		**Prior ECP Use**		**Total N=540** ***No. (%)***
	= 16 N=22	**= 17 N=518**	**< HS N=64**	**= HS N=476**	**Ever N=213**	**Never N=327**	
Total Correct Use, no. (%)	17 (77.3)	349 (67.4)	43 (67.2)	323 (67.9)	142 (66.7)	224 (68.5)	**366 (67.8)**
Total Incorrect Use, no. (%)	3 (13.6)	137 (26.4)	16 (25.0)	124 (26.1)	63 (29.6)	77 (23.5)	**140 (25.9)**
Intentional†	0	1.4	0	1.5	1.9	0.9	7 (1.3)
Unintentional‡	13.6	25.1	25.0	24.6	27.7	22.6	**133 (24.6)**
Missing data	9.1	6.2	7.8	6.1	3.8	8.0	34 (6.3)
Timing for the first pill after sex act							
> 72 hours	0	1.9	0	2.1	1.9	1.8	10 (1.9)
< 72 hours	86.4	92.7	87.5	93.1	95.3	90.5	**499 (92.4)**
Missing data	13.6	5.4	12.5	4.8	2.8	7.6	31 (5.7)
Interval between the second and first pill							
</> 12 hours	13.6	25.7	25.0	25.2	29.1	22.6	136 (25.2)
At 12 hours	81.8	71.2	70.3	71.8	68.5	73.7	**387 (71.7)**
Missing data	4.5	3.1	4.7	2.9	2.3	3.7	(3.1)

Data were extracted from the sponsor's Tables 5.8c, 5.8f and 5.8g in page 133-137 of vol. 28.
† "Intentional" was that subjects correctly recognized the instruction before use;
‡ "Unintentional" was that subject incorrectly recognized the instruction before use.

Table 21b. **Incorrect Use of Plan B by Primary Definition**
(% of subjects who used the product, **excluding** those who provided insufficient data from denominator)

	Age (years)		**Education**		**Prior ECP Use**		**Total** *No. (%)*
	= 16	**= 17**	**< HS**	**= HS**	**Ever**	**Never**	
Valid Users*	**20**	**486**	**59**	**447**	**207**	**301**	**506**
Total Correct Use, no. (%)	17 (85.0)	349 (71.8)	43 (72.9)	323 (72.2)	142 (68.6)	224 (74.4)	**366 (72.3)**
Total Incorrect Use, no. (%)	3 (15.0)	137 (28.2)	16 (27.1)	124 (27.7)	63 (30.4)	77 (25.6)	**140 (27.7)**
Intentional†	0	1.4	0	1.6	1.9	1.0	7 (1.4)
Unintentional‡	15.0	26.7	27.1	26.2	28.5	24.6	**133 (26.3)**
Timing for the first pill after sex act							
> 72 hours	0	2.1	0	2.2	1.9	2.0	10 (2.0)
< 72 hours	95.0	98.8	94.9	99.1	98.1	98.3	**499 (98.6)**
Interval between the second and first pill							
</> 12 hours	15.0	27.4	27.1	26.8	30.0	24.6	136 (26.9)
At 12 hours	90.0	75.9	76.3	76.5	70.5	80.0	**387 (76.5)**

Data were reprocessed based on the sponsor's Tables 5.8c,f,g, 5.10a in page 133-140 of vol. 28.
* "Valid users" were subjects who used the product and provided sufficient data: Valid Users = (Total Users – Users with missing data).
† "Intentional" was that subjects correctly recognized the instruction before use;
‡ "Unintentional" was that subject incorrectly recognized the instruction before use.

Incorrect Use Analysis with Alternative Criteria: The sponsor re-analyzed the data using alternate criteria (different dosing regimens), as summarized in Table 22a, which decreased the incorrect use from 27% to 2%. The sponsor did not provide any evidence in the submission to support if the alternate criteria/dosing regimens produced comparable efficacy to the labeled dosing regimen (both in Rx and the proposed OTC label). There was also no explanation as to why the number of subjects with insufficient data varied from 34-42 among the different analyses.

In a pivotal efficacy trial (WHO trial) submitted to the original Plan B NDA (*the trial # was not provided*), the time interval between the 1st pill and 2nd pill was variable (Table 22b) and "high effectiveness" was obtained, as the sponsor quoted in the report.

Table 22a. **Incorrect Use of Plan B by Different Criteria**
(% of 540 enrolled subset population who used the product)

	Primary Criteria†	**Alternate Criteria I‡**	**Alternate Criteria II***	**Alternate Criteria III#**
Dosing Regimen	1st pill <72 hrs 2nd pill =12 hrs	1st pill <72 hrs 2nd pill <16 hrs	1st pill <72 hrs 2nd pill 6-18 hrs	1st pill <120 hrs 2nd pill <24 hrs
Subjects with Insufficient Data No. (%)	34 (6.7)	40 (7.4)	39 (7.2)	42 (7.7)
Incorrect Use No. (%)	140 (25.9)	33 (6.1)	32 (5.9)	10 (1.9)
Correct Use No. (%)	366 (67.8)	467 (86.5)	469 (86.9)	488 (90.4)

† Data were extracted from Table 5.8a (vol. 28, p131); ‡ from Table 5.11a (vol. 28, p141); * from Table 5.14a (vol. 28, p151); # from Table 5.17a (vol. 28, p160a).

Table 22b. **Comparison of Dosing Interval of Second Pills between Current Study and Previous Clinical Trial (submitted to the original NDA)**

Time Interval between 1st pill and 2nd pill	**Current AU Study N=540 No. (%)**	**WHO Trial* N=974 (%)**
<12 hours	52 (9.6)	(9)
At 12 hours	387 (71.6)	(74)
12-16 hours	63 (11.7)	(13)
> 16 hours	21 (3.9)	(5)

* The sponsor reanalyzed the data submitted to the original NDA. No details were provided in the report; data were % only.

Consultation with Health Care Providers

At Admission: Of the 585 enrolled subjects, 92 (16%) consulted with clinician or pharmacist at the initial study visit (right after enrollment). The most common questions that these subjects asked were related to safety and contraindications (5.8%) and instructions for use (3.1%) (Table 23a).

During Plan B Use: Thirty-one (6%) subjects who used Plan B consulted a health care provider for the reasons listed in Table 23b. It is unknown if these 31 subjects were part of the 92 who consulted at the initial study visit.

Incorrect and contraindicated uses after consultation: Consultation with health care providers tended to increase contraindicated use and decrease incorrect use (Table 23c). It appears that the 85 subjects in Table 23c who consulted a healthcare provider had used Plan B and had provided enough information for this analysis. It is unclear that all subjects who consulted a healthcare provider actually used Plan B.

Table 23a. **Consultation with Clinician or Pharmacist at Admission**
(% of enrolled population)

	Clinical Sites N=550	**Pharmacy Sites N=35**	**All Sites N=585**
Consulted Subjects	14.9	28.6	15.7
Consulted Topics			
Safety	5.6	8.6	5.8
Instruction (use)	3.3	0	3.1
Take with food	2.2	2.9	2.2
Other contraception	1.8	0	1.7
Products	1.3	8.6	1.7
Efficacy	1.3	5.7	1.5

Data were extracted from the sponsor's Table 1.5 in page 020 of vol. 28.

Table 23b. **Consultation with Health Care Providers during Study**
(% of enrolled population who provided any follow-up data)

Consultation	Clinical Sites N=522	Pharmacy Sites N=31	Total N=553
Yes (total 31 users)	5.0	16.1	5.6
Reasons			
Contraindication question	0.2	0.0	0.2
Informed Physician	1.3	9.7	1.8
Medical problem or side effect	1.5	3.2	1.6
Nonspecific questions	0.2	0.0	0.2
Ongoing contraception	0.8	3.2	0.9
Pregnancy test (+)	0.2	6.5	0.5
Question about Plan B	0.6	0.0	0.5
Repeat ECP use	0.6	0.0	0.5
Routine appointment	0.2	6.5	0.5
Wanted pregnancy test	0.2	0.0	0.2

Data were extracted from Table 6.9 (vol. 28, p218)

Table 23c. **Contraindicated and Incorrect Use of Plan B by Subjects Who Consulted/did not Consult Health Care Provider**

Plan B Use	Consultation with Health Care Provider		Total Users N=540 N0. (%)	*P* value
	Yes N=85 No. (%)	No N=455 No. (%)		
Contraindicated use	3 (3.5)	4 (0.9)	7 (1.3)	0.08
Incorrect Use				
Primary criteria	16 (18.8)	124 (27.3)	140 (25.9)	0.21
Alternate I	3 (3.5)	30 (6.6)	33 (6.1)	0.45
Alternate II	3 (3.5)	29 (6.4)	32 (5.9)	0.45
Alternate III	0 (0)	10 (2.2)	10 (1.9)	0.37

Data were extracted from Table 23 in the *Addendum to Final Study Report*, p27

Pregnancy and Menstrual Period

Menstrual Period Status after Plan B (Table 24a): Of the 540Plan B users, 513 (95%) had a menstrual period before the end of their study participation. The median time of onset of the menstrual period was 6 days (0-49 days) after product use (2nd pills).

Table 24a. **Menstrual pattern after first use of Plan B**

Menstrual Period Onset	Age (years)		Total N=540
	= 16 N=22	= 17 N=518	
% of Users			
Yes	81.8	95.6	95.0
No	18.2	4.1	4.6
Missing	0	0.4	0.4
Days after the first pill			
Mean ± SD (Range)	13.3±11.8 (1-40)	10.3±8.4 (0-49)	10.4±8.5 (0-49)
Median	8	7	7

Data were extracted from Table 6.8b (vol. 28, p217).

Pregnancy after Plan B (Tables 24b and 24c): Of the 540 users , 58 met the criteria for pregnancy review by the medical monitor from Family Health International. Ten were confirmed to be pregnant and at least some may have been pregnant prior to using Plan B. All 10 pregnant subjects took the first pill within 72 hours after sex and the second pill at 12 or 13 hours after the first pill. Their characteristics are summarized in Table 24c.

The sponsor reported a 1.9% pregnancy rate for this study population (10 of 540). However, there were 14 “unclassifiable” pregnant subjects who did not complete the follow-up. The maximal possible pregnancy rate for the study subjects was 4.4% (10+14 of 540), so the true pregnancy rate was from 1.9% to 4.4%.

Table 24b. **Pregnancy in the enrolled subjects who use Plan B**

	Subject		
	Number	**%**	
Total Users	540	100	
Suspected Pregnancy	58	10.7	
Classifiable Pregnancy	10	**1.9**	**4.4%**
Unclassifiable Pregnancy	14	2.6	

Data were extracted from the text of the report (vol. 27, p059). Classifiable and unclassifiable pregnancy was determined by the medical monitor from FHI; unclassifiable pregnancy was due to insufficient data because of only one follow-up contact.

Table 24c. **Characteristics of the 10 Classifiable Pregnant Subjects**

Subject ID	Age (yr)	Marital Status	Education	Prior EC Use	Race	Ethnicity
4072	17	Single	HS	Yes	African-American	Non- Hispanic
2123	18	Single	= HS	No	White	Non- Hispanic
1058	19	Single	= HS	No	White	Non- Hispanic
2042	19	Single	= HS	Yes	White	Non- Hispanic
2065	22	Single	= HS	No	White	Non- Hispanic
5058	23	Single	= HS	Yes	White	Non- Hispanic
3037	25	Single	= HS	Yes	White	Non- Hispanic
5098	26	Single	= HS	No	White	Non- Hispanic
3057	32	Single	= HS	No	White	Non- Hispanic
6021	36	Single	= HS	No	African-American	Non- Hispanic

Data were extracted from Listing 9 (vol. 29, p016-017)

Adverse Events (AEs)

There were no new safety signals for Plan B noted during this study. Of the 540 subjects who used the study product, 246 (46%) reported at least one adverse event. There was a total of 412 AEs.

AE reports = 1.0 % of enrolled subjects who used Plan B were summarized in Table 25a from both data collection sources. AEs presented by body system are listed in Table 25b. The most common AEs occurred in the digestive and nervous systems and were abdominal pain, nausea, headache, and asthenia.

***Table 25a.* Common Adverse Event Reports**
(AEs = 1.0 % of enrolled subjects who used the study product)

Adverse Events	Total AEs from both Sources† (%)	AEs from Follow-up Contact (%)‡
Abdominal pain	14.3	8.9
Nausea	12.4	9.4
Headache	11.3	4.3
Asthenia	8.0	3.7
Metrorrhagia	4.3	2.4
Dizziness	3.7	1.9
Breast Pain	2.8	1.9
Pharyngitis	2.6	ND
Menorrhagia	1.9	1.7
Emotional Liability	1.7	0.9
Somnolence	1.5	ND
Vaginal Hemorrhage	1.3	0.6
Diarrhea	1.3	0.9
Vomiting	1.1	0.6
Allergic reaction	1.1	ND
Total Subjects with AEs	246/540 (45.6%)	150/540 (27.8%)

† Total AEs were pooled from the Study Data Card and the follow-up contacts; the data were extracted from Table 6.1a (vol. 28, p170-172)
‡ Data were extracted from Table 6.2a (vol. 28, p185); ND: no data available in the Table.

Table 25b. **Adverse Event Reports by Body System**
(% of enrolled subjects who used the study product, n=540)

Body System	Total AEs from both Sources† (%) N=246	AEs from Follow-up Contact (%)‡
Body as a whole	37.6	16.9
Digestive System	16.5	11.5
Urogenital System	14.8	7.4
Nervous System	9.1	3.0
Respiratory System	5.4	ND
Skin and Appendages	0.6	0.4
Cardiovascular System	0.4	0.2
Special Senses	0.4	0.2
Hemic and Lymphatic System	0.2	ND

† Total AEs were pooled from the Study Data Card and the follow-up contacts, extracted from Table 6.3a (vol. 28, p192) and Table 6.5a (vol. 28, p203); the number of Plan B users who reported AEs from both sources was 246 (45.6% of 540 users). A subject may have more than one category of AEs.
‡ Data were extracted from Table 6.6b (vol. 28, p207); the number of subjects who reported AEs based on the follow-up contact only was 150 (27.8% of 540 users).
ND: data were not available in the report.

The pattern of Plan B -related AEs was similar across subgroups defined by ethnicity, race, and education (Table 25c). The users <16 years old tended to report fewer AEs than those ages 17 years and above; however, the sample size in the age <16 subgroup was quiet small (n=22).

The AE reports were comparable between correct and incorrect users. The contraindicated users tended to report more AEs; however, the sample size of contraindicated users were too small (n=7) for a meaningful comparison.

Of all 412 AEs, 52.7% (217) were determined to be Plan B related Regarding severity, 85% of 412 AEs were mild and 15% moderate. There were no serious AE reports. Approximately 33% of AEs were treated with either prescription or OTC medication. Ninety-eight percent of subjects stated that the AEs would not stop them from using the product in future.

Table 25c. **Adverse Event Reports among demographic subgroups**
(% AEs of enrolled subjects who use the product in each subgroup)

Subjects	Total AEs from both Sources (%)†	AEs from Follow-up Contacts (%)‡
Overall % in all users, n=540	45.6	27.8
Age (years)		
< 16, n=22	31.8	13.6
> 17, n=518	46.1	28.4
Ethnic Hispanic		
Yes, n=76	51.3	28.9
No, n=461	44.7	27.8
Race		
White, n=397	43.8	27.2
Non-White, n=100	51.0	28.0
Education Level		
< high school, n=64	37.5	20.3
= High school, n=476	46.6	28.8
Eligibility Status		
Eligible users, n=533	45.8	28.1
Ineligible users, n=7	28.6	0
Previous EC Use		
Ever, n=215	44.0	27.4
Never, n=325	46.6	28.0
Use Correctness[#]		
Correct users, n=393*	45.8	ND
Incorrect users, n=142	43.7	ND
Contraindicated users, n=7	57.1	ND

† Total AEs were pooled from the Study Data Card and the follow-up contacts; the data were extracted from Table 6.1b-g (vol. 28, p173-184)

‡ Data were extracted from Table 6.2b- (vol. 28, p186-191); ND: data were not available in the report.

* % AE subjects in the correct users: total numbers of users with AEs = 246/540, incorrect users with AEs = 62/140 and contraindicated users with AEs =4/7; the total correct users = 393 (540-140-7).

AEs in the contraindicated users were from Table 6.4b (vol. 28, p201) and Table 6.5b (vol. 28, p204); and AEs in the incorrect users were from Table 6.4c (vol. 28, p202) and Table 6.5c (vol. 28, p205).

Concomitant Medications and Allergic Reactions

No subjects reported allergies to Plan B. Medications taken before and after the first screening and allergic reactions are summarized in Table 26. Of the 543 subjects who provided any follow-up data, 36.6% took at least one other medication and 19% reported allergies to at least one medication other than Plan B.

Table 26. **Medications and allergy**
(% of enrolled population)

	Previous Week At the 1st Screening† N=585	**After 1st Screening (Follow-up Contacts)‡ N=543**
Medications Taken		
Subjects (%)	42.9	36.6
Total #	140	114
Medication Allergy	No data	19.0*

† Extracted from the sponsor's Table 3.1a-b (page 070-078 of vol.28);
‡ Extracted from the sponsor's Table 3.3a-b (page 087-092 of vol. 28);
* Extracted from the sponsor's Table 2.12 (page 067 of vol. 28).

Behavior Changes

Sexual activity: Sexual activity and contraceptive methods before and after Plan B use are summarized in Table 27a. The results presented were based on the 543 subjects who provided follow-up data after the first screening. After Plan B, subjects used condoms more and the withdrawal method less. Sexual activity decreased from 100% within the month before screening to 62% after screening. Unprotected sexual intercourse, or "At least one sex act without contraception", decreased from 60% before screening to 20% after screening. A comparison of he unprotected sexual intercourse information among the different demographic subgroups after enrollment was not available in the report.

Contraception methods: Table 27b shows changes in contraception methods between pre- and post-Plan B in different demographic subgroups, based on the 502 subjects who provided follow-up contact data at = 28 days. A slight increase in condom use and decrease in withdrawal method were noted after screening.

Multiple Uses: Ten (1.7%) of the 585 enrolled women had multiple enrollments (8 for twice and 2 for 3 times). The 10 subjects, ages 17-25 years, were eligible at all screenings and received the study product at each screening. Second screenings occurred between 4-80 days (media 8 days). Multiple screenings occurred at all sites except the Seattle clinic and the pharmacies. Eight of 10 subjects used Plan B; 2 (enrolled twice) lost contact. Six

of a total of 18 uses (twice for 6 subjects and 3 times for 2 subjects) were incorrect because of the incorrect use of the 2nd pill.

As seen in Table 27c, compared to the "once" users, more multiple users had "at least one unprotected sex" (88% vs. 59%), and used the "withdrawal" method (50% vs. 27%), but more multiple users used "condoms" (88% vs. 79%) and did not have previous EC use experience (75% vs. 60%). However, the sample size of the subset of multiple users was too small to make an accurate assessment of contraceptive behaviors.

Table 27a. **Sexual activity and Contraception before and after Plan B Use**
(% of the screened subjects who provided any follow-up data)

Sex and Contraception	**Before First Screening† N=543**	**After First Screening‡ N=543**
Subjects who had Sex	100.0	61.9 (336)
At least one sex w/o contraception	59.7 (324)	19.6* (66)
Contraception Methods		
Condoms	79.0	89.6
Withdrawal	27.6	10.1
Oral contraceptives	21.9	20.5
Spermicide	8.7	10.7
Natural family planning	2.2	0.3
Emergency contraceptives	1.7	1.2
DepoProvera or Lunelle	1.5	1.2
Other	0.2	1.2

Data were extracted from Tables 7.1a and 7.1b (vol. 28, p219-220); a subject may have used more than one method. Data in the parentheses are the number of subjects.
† Data collected from the month before the first screening;
‡ Data collected from all follow-up contacts after the first screening.
* % of subjects who had sex acts.

Table 27b. **Changes in Contraception Methods before and after First Screening by Demographics**
(% of enrolled subjects who provided any follow-up data at = 28 days)

	Sexual Activity		Switching in Effective Methods			Switching in Condom use		
	One month before Screening	between Screening and End of follow-up	Less? More	More? Less	More effective before and after†	? use no condom	? use condom	Used condom before and after†
Enrolled subjects, n=502	(502) 100	319 (63.5)	36 (11.3)	26 (8.2)	37 (11.6)	15 (4.7)	33 (10.3)	251 (78.7)
Age (years)								
= 16, n=22, no. (%)	22 (100)	14 (63.6)	4 (28.6)	0	1 (7.1)	0	0	14 (100)
=17, n=480, no. (%)	480 (100)	305 (63.5)	32 (10.5)	26 (8.5)	36 (11.8)	15 (4.9)	33 (10.8)	237 (77.7)
Ethnic Hispanic								
Yes, n=70	70 (100)	45 (64.3)	5 (11.1)	3 (6.7)	7 (15.6)	1 (2.2)	8 (17.8)	33 (73.3)
No, n=429	429 (100)	273 (63.6)	31 (11.4)	23 (8.4)	30 (11.0)	14 (5.1)	25 (9.2)	217 (79.5)
Race								
White, n=373	373 (100)	226 (60.6)	26 (11.5)	16 (7.1)	26 (11.5)	10 (4.4)	25 (11.1)	179 (79.2)
Non-White, n=94	94 (100)	69 (73.4)	6 (8.7)	8 (11.6)	9 (13.0)	4 (5.8)	9 (5.8)	54 (78.3)
Education								
< High school, n=60	60 (100)	37 (61.7)	8 (21.6)	2 (5.4)	5 (13.5)	3 (8.1)	3 (8.1)	31 (83.8)
= High school, n=442	442 (100)	282 (63.8)	28 (9.9)	24 (8.5)	32 (11.3)	12 (4.3)	30 (10.6)	220 (78.0)
Prior ECP Use								
Ever, n=195	195 (100)	127 (65.1)	12 (9.4)	13 (10.2)	12 (9.4)	6 (4.7)	15 (11.8)	94 (74.0)
Never, n=307	307 (100)	192 (62.5)	24 (12.5)	13 (6.8)	25 (13.0)	9 (4.7)	18 (9.4)	157 (81.8)

Data were extracted from the sponsor's Tables 7.2a-g (p221-227 of vol. 28), which covered from one month before first screening to the end of follow-up contacts. Any of the following was defined as "more effective methods": oral contraceptive pills, Depo-Provera, Lunelle, vasectomy, IUD; otherwise, as "less effective methods". † % of subjects who had sex during study (between screening and end of follow-up); "before" – one month before screening and "after" – end of follow-up contacts (= 28 days).

Table 27c. **Demographics and Contraceptive Behavior of subjects with multiple screening and using Plan B**

Characteristics	Screened		Used	
	Once N=655	Multiple N=10	Once N=532	Multiple N=8
Age (years)				
<16	31 (4.7)	1 (10.0)	22 (4.1)	0
17-25	497 (75.9)	8 (80.0)	398 (74.8)	7 (87.5)
26-30	84 (12.8)	1 (10.0)	77 (14.5)	1 (12.5)
Marital status				
single	585 (89.3)	10 (100)	472 (88.7)	8 (100)
married	37 (5.6)	0	31 (5.8)	0
Education				
8th grade or less	3 (0.5)	0	2 (0.4)	0
9th-11th grade	90 (13.7}	2 (20.0)	61 (11.5)	1 (12.5)
high school/GED	91 (13.9)	2 (20.0)	70 (13.2)	2 (25.0)
vocational/technical school	11 (1.7)	0	9 (1.7)	0
Some college	317 (48.4)	4 (40.0)	268 (50.4)	3 (37.5)
finished college	105 (16.0)	1 (10.0)	89 (16.7)	1 (12.5)
graduate school	37 (5.6)	1 (10.0)	33 (6.2)	1 (12.5)
missing	1 (0.2)	0	0	0
Previous EC use				
No	347 (53.0)	8 (80.0)	321 (60.3)	**6 (75.0)**
Yes	234 (35.7)	2 (20.0)	211 (39.7)	2 (25.0)
Once	151 (23.1)	1 (10.0)	137 (25.8)	1 (12.5)
Twice	60 (9.2)	1 (10.0)	55 (10.3)	1 (12.5)
Contraception methods in previous month				
OC pills	123 (18.8)	2 (20.0)	118 (22.2)	1 (12.5)
Condoms	458 (69.9)	**8 (80.0)**	420 (78.9)	**7 (87.5)**
Spermicide	49 (7.5)	0	47 (8.8)	0
DepoProvera or Lunelle	10 (1.5)	0	8 (1.5)	0
Withdrawal	160 (24.4)	5	145 (27.3)	**4 (50.0)**
Natural fam. planning	12 (1.8)	0	12 (2.3)	0
EC pills	13 (2.0)	0	9 (1.7)	0
Other	1 (0.2)	0	1 (0.2)	0
At least one unprotected sex	346 (52.8)	**8 (80.0)**	315 (59.2)	**7 (87.5)**

Data were extracted from the sponsor's tables 8.2, 8.3, 8.4, 8.5 (p229-234 of vol28); only corresponding screening data to multiple use were presented.
The numbers in parentheses are % of the screening subjects in "Screening" population, or % of the users in "Used" (subjects who used Plan B during study).

SUMMARY

1. **Study Design:**

   This was an open-label, single-arm, multi-center clinical trial conducted in 5 family planning clinic sites across 5 states in the United States and 5 pharmacy stores in Washington State to assess self-selection, self-administration (use), safety and efficacy of Plan B in an OTC-like setting. Of 665 women screened, 585 (88%) were enrolled (age 14-44 years) and received one package of Plan B, and 540 (92%) used Plan B.

2. **Data Collection:**

   All data were collected by pre-designed questionnaires and study data cards (diary card). Screening and background data were obtained in person at study sites; follow-up contacts were conducted by phone (98% of contacts) or in person (2% of contacts); and the study data card was received by mail. The follow-up contact data were superior to the diary card for the actual data analyses (except AEs). Five hundred two (86%) of the 585 enrolled subjects completed 2 follow-up contacts (45% per-protocol which was the first contact at 5-8 days and the second contact at = 28 days; 41% off-protocol).

   Less compliance with follow-up was noted in subjects at age 14-16 and subjects with less than high school education. The compliance in subjects for other demographic characteristic (races, ethnicity and history of emergency contraception use) appeared to be comparable.

3. **Results**:

   Self-selection and Self-deselection:

   Approximately 95% of subjects who used Plan B could correctly self-select, and 1.3% of subjects with contraindications used Plan B (pregnancy, unexplained vaginal bleeding).

   Results on subjects who did not use Plan B in the study were not reported.

   Correct/Incorrect use:

   Overall correct use (time to take first and second pills) of Plan B in the study population was 67.8% (366 of 540 total users) and incorrect use was 28%-32% (in-/excluding subjects with missing data).

   Correct use for the first pill was 92.4% and for the second pill was 71.7%. The majority (95%) of incorrect use was unintentional.

There were no significant differences in incorrect uses among subjects with different ages, educational levels, previous EC experience and ethnicities/races.

Pregnancy rate after Plan B:

Ten of 540 subjects (1.9%) were pregnant. They were ages 17-36: 9 had at least a high school education; 8 were white and 2 African-American; all were non-Hispanic; and 4 had previous EC experience.

By including the 14 unclassifiable pregnant subjects who did not complete the follow-up and from whom the outcomes were unknown, the pregnancy rate would be 4.4%.

Sexual and contraceptive behaviors:

The following behavioral changes (as a secondary objective) were monitored during the 4-week follow-up:

Sexual Activity:	Decreased from 100% (before study) to approximately 64% (during study) (Table 27b);
Unprotected sex:	"At least one sex act without contraception" decreased from 60% (before study) to 20% (during study) (Table 27a);
Condom Use:	Increased from 79% (before) to 90% (after) and withdrawal decreased from 28% (before) to 10% (after) (Table 27a);
Routine Contraception:	No increase in switching to less-effective contraception methods (Table 27b);
Multiple Use:	Ten (1.7%) of the 585 enrolled subjects re-enrolled and received Plan B more than once (8 used twice and 2 used 3 times). There were no significant differences in contraceptive behaviors between the multiple users and the single users.

However, this AU study was not primarily designed for assessment of potential risk behaviors in consumers who may use Plan B in an OTC setting.

Adverse events:

There were no serious adverse events (AEs) reported in the 585 enrolled subjects from the actual use study and no new safety signals for Plan B were noted in this study. The most common AEs were abdominal pain, nausea, headache and asthenia; 85% of AEs were mild and 15% moderate. Most AEs resolved without any medical intervention and 30% were treated with either prescription or OTC medication.

Comparison between age 14-16 and 17-44:

Approximately 5% (29 of 585) of subjects age 14-16 were enrolled in the study and 22 of them used Plan B.

The overall *incorrect use, contraindicated use, AEs and negative behavior changes* were not increased in subjects age 14-16, as compared to those at least 17 years old. (Table 28).

The follow-up compliance rate was lower in the subjects age 14-16 years than those in ages = 17 years, with lost-to-contact 24% vs. 7% and 2 contacts 55% vs. 87%.

Comparison among educational levels:

There were 0.3% (2 of 585) of subjects with = 8^{th} grade education and 13% (76 of 585) of subjects with a 9^{th} – 11^{th} grade education.

Subjects with less education compared with subjects with at least a high school education, correctly self-selected and used this product and had similar contraception usage and AEs (Table 29). These data was obtained mainly from subjects at education level of 9^{th}-11^{th} grade.

Comparison between Ever and Never previous EC use:

There were no significant differences in *incorrect use, contraindicated use, AEs and contraception usage* between the 40% of subjects with, and the 60% without, previous EC experience (Table 30).

The subjects with previous EC use experience were more likely to have "at least one act of unprotected sexual intercourse" and tended to use condoms less in the month prior to enrollment (Table 15).

More subjects with prior EC experience requested and used Plan B in this study with the reasons "unprotected sex" or "used no contraception" (Table 30).

Table 28. **Comparison in Plan B use between age 14-16 and age 17-44**
(% of the enrolled subjects; otherwise % of users †)

Parameters	**Age (years)**		**Total**
	14-16	**17-44**	***No. (%)***
Enrolled Subjects, *No (%)*	29 (49.6%)	556 (95.0%)	585
Subjects used Plan B, *No. (%)*	22 (75.9%)	518 (93.2%)	540 (92.3)
Compliance of follow-up contacts			
Lost Follow-up	24.1	6.5	43 (7.4)
One Follow-up	20.7	4.1	29 (5.0)
Two Follow-up	55.2	87.2	501 (85.6)
> 3 Follow-up	0	2.2	12 (2.1)
Prior EC Use	27.6	40.6	234 (40.0)
Education 8^{th} Grade and less	3.4	0.2	2 (0.3)
$9^{th} – 11^{th}$ Grade	96.6	8.6	76 (13.0)
HS above	0	91.2	507 (86.7)
Reason to Request Plan B			
Condom broke or slipped	31.0	37.8	219 (37.4)
Unprotected sex	27.6	33.5	194 (33.2)
Prevent pregnancy	27.6	16.4	99 (16.9)
OCP problem	3.4	4.0	23 (3.9)
Mistake/accident	6.9	2.0	13 (2.2)
Contraceptive failure (unspecified)	0.0	1.8	10 (1.7)
Withdrawal	0.0	1.4	8 (1.4)
Prevention, unspecified	3.4	1.1	7 (1.2)
Reason to Use Plan B†			
Condom broke/slipped	54.5	44.8	244 (45.2)
Used no contraception	27.3	40.2	214 (39.6)
Missed OCPs	9.1	6.8	37 (6.9)
Withdrawal	9.1	3.3	19 (3.5)
Disposition of Plan B			
Took both pills	75.9	93.0	
Time taken 1^{st} pill (hours after sex)	40.2±19.2 [11.5-70]	34.6±21.2 [-103-175]	34.8±21.1 [-103-175]
Time taken 2^{nd} pill (hours after 1^{st} pill)	12.1±0.5 [11-14]	12.5±3.3 [0-36]	12.5±3.2 [0-36]
Contraindicated Use†	4.5	1.2	7 (1.3)
Pregnancy before Plan B	0	0.2	1 (0.2)
Unexplained vaginal bleeding	4.5	1.0	6 (1.1)
Allergy to Plan B	0	0	0
Correct/Incorrect use†			
Overall Correct Use	77.3	67.4	366 (67.8)
Overall Incorrect Use	13.6	26.4	140 (25.9)
Overall Incorrect use (+missing data)	22.7	32.6	174 (32.2)
Correct use of 1^{st} pill (<72 hr)	86.4	92.7	499 (92.4)
Correct use of 2^{nd} pill (12 hr)	81.8	71.2	387 (71.7)
Adverse Events†			
From all sources; Subjects with AEs	31.8	46.1	246 (45.6)
Behavior change (% of subjects with sex)			
Sex act before study (one month)	100.0	100.0	502 (100.0)
Sex acts during study (4 weeks)	63.6	63.5	319 (63.5)
Change to more effective contraception	28.6	10.5	36 (11.3)
Change to less effective contraception	0	8.5	26 (8.2)
Change to condom use	0	10.8	33 (10.3)
Change to no condom use	0	4.9	15 (4.7)

Table 29. **Comparison in Plan B use between Subjects < HS and = HS Education**
(% of the enrolled subjects; otherwise % of users †)

Parameters	Education*		Total *No. (%)*
	< HS	= HS	
Enrolled Subjects, *No (%)*	78 (13.3%)	507 (86.7%)	585
Subjects used Plan B, *No. (%)*	64 (82.1%)	476 (88.1%)	540 (92.3)
Compliance of follow-up contacts			
Lost Follow-up	19.2	5.5	43 (7.4)
One Follow-up	11.5	3.9	29 (5.0)
Two Follow-up	66.7	88.6	501 (85.6)
> 3 Follow-up	2.6	2.0	12 (2.1)
Prior EC Use	12.4	87.6	234 (40.0)
Reason to Request Plan B			
Condom broke or slipped	34.6	37.9	234 (40.0)
Unprotected sex	23.1	34.7	2 (0.3)
Prevent pregnancy	28.2	15.2	76 (13.0)
OCP problem	5.1	3.7	507 (86.7)
Mistake/accident	3.8	2.0	
Contraceptive failure (unspecified)	0.0	2.0	219 (37.4)
Withdrawal	2.6	1.2	194 (33.2)
Prevention, unspecified	2.6	1.0	99 (16.9)
Reason to Use Plan B†			23 (3.9)
Condom broke/slipped	46.9	45.0	13 (2.2)
Used no contraception	28.1	41.2	10 (1.7)
Missed OCPs	10.9	6.3	8 (1.4)
Withdrawal	7.8	2.9	7 (1.2)
Disposition of Plan B			
Took both pills	82.1	93.7	
Time taken 1st pill (hours after sex)	35.0±18.1 [5-70]	34.8±21.5 [-103-175]	34.8±21.1 [-103-175]
Time taken 2nd pill (hours after 1st pill)	12.9±3.0 [11-24.5]	12.5±3.2 [0-36]	12.5±3.2 [0-36]
Contraindicated Use†	1.6	1.3	7 (1.3)
Pregnancy before Plan B	0	0.2	1 (0.2)
Unexplained vaginal bleeding	1.6	1.1	6 (1.1)
Allergy to Plan B	0	0	0
Correct/Incorrect use†			
Overall Correct Use	67.2	67.9	366 (67.8)
Overall Incorrect Use	25.0	26.1	140 (25.9)
Overall Incorrect use (including subjects with missing data)	32.8	32.2	174 (32.2)
Correct use of 1st pill (<72 hr)	87.5	93.1	499 (92.4)
Correct use of 2nd pill (12 hr)	70.3	71.8	387 (71.7)
Adverse Events†			
From all sources; Subjects with AEs	37.5	46.6	246 (45.6)
Behavior change (% of subjects with sex)			
Sex act before study (one month)	100.0	100.0	502 (100.0)
Sex acts during study (4 weeks)	61.7	63.8	319 (63.5)
Change to more effective contraception	21.6	9.9	36 (11.3)
Change to less effective contraception	5.4	8.5	26 (8.2)
Change to condom use	8.1	10.6	33 (10.3)
Change to no condom use	8.1	4.3	15 (4.7)

* "< HS": includes 8th grade (0.3%, 2 of 585) and 9th-11th grade (13%, 76 of 585).

Table 30. **Comparison in Plan B use between Subjects with and without Prior EC Use**
(% of the enrolled subjects; otherwise % of users †)

Parameters	Prior EC Use		Total
	Ever	Never	*No. (%)*
Enrolled Subjects, *No (%)*	234 (40.0%)	351 (60.0%)	585
Subjects used Plan B, *No. (%)*	213 (91.0)	327 (93.2%)	540 (92.3)
Compliance of follow-up contacts			
Lost Follow-up	9	6.3	43 (7.4)
One Follow-up	4.7	5.1	29 (5.0)
Two Follow-up	85.0	86.0	501 (85.6)
> 3 Follow-up	1.3	2.6	12 (2.1)
Reason to Request Plan B			
Condom broke or slipped	32.5	40.7	234 (40.0)
Unprotected sex	37.6	30.2	2 (0.3)
Prevent pregnancy	18.8	15.7	76 (13.0)
OCP problem	3.8	4.0	507 (86.7)
Mistake/accident	2.1	2.3	
Contraceptive failure (unspecified)	1.7	1.7	219 (37.4)
Withdrawal	0.0	2.3	194 (33.2)
Prevention, unspecified	0.9	1.4	99 (16.9)
Reason to Use Plan B†			23 (3.9)
Condom broke/slipped	39.9	48.6	13 (2.2)
Used no contraception	44.6	36.4	10 (1.7)
Missed OCPs	7.0	6.7	8 (1.4)
Withdrawal	3.8	3.4	7 (1.2)
Disposition of Plan B			
Took both pills	91.0	92.9	
Time taken 1st pill (hours after sex)	34.1±18.7 [-12.5-88]	35.3±22.7 [-103-175]	34.8±21.1 [-103-175]
Time taken 2nd pill (hours after 1st pill)	12.6±3.1 [0-36]	12.5±3.2 [0-36]	12.5±3.2 [0-36]
Contraindicated Use†	1.4	1.2	7 (1.3)
Pregnancy before Plan B	0	0.3	1 (0.2)
Unexplained vaginal bleeding	1.4	0.9	6 (1.1)
Allergy to Plan B	0	0	0
Correct/Incorrect use†			
Overall Correct Use	66.7	68.5	366 (67.8)
Overall Incorrect Use	29.6	23.5	140 (25.9)
Overall Incorrect use (including subjects with missing data)	33.4	31.5	174 (32.2)
Correct use of 1st pill (<72 hr)	95.3	90.5	499 (92.4)
Correct use of 2nd pill (12 hr)	68.5	73.7	387 (71.7)
Adverse Events†			
From all sources; Subjects with AEs	44.0	46.6	246 (45.6)
Behavior change (% of subjects with sex)			
Sex act before study (one month)	100.0	100.0	502 (100.0)
Sex acts during study (4 weeks)	65.1	62.5	319 (63.5)
Change to more effective contraception	9.4	12.5	36 (11.3)
Change to less effective contraception	10.2	6.8	26 (8.2)
Change to condom use	11.8	9.4	33 (10.3)

COMMENTS

1. The majority (94%) of subjects were recruited from family planning clinics. This may not be representative of the target population in an OTC setting. However, it would have been impractical, if not impossible, for the sponsor to have used traditional recruiting procedures (mall intercepts, etc.).

2. Subjects were observed for only 4 weeks after Plan B was dispensed in this study. This limited follow-up duration would only provide data regarding short-term contraceptive usage.

3. Most incorrect use was due to not taking the 2nd pill at 12 hours after the first pill. Efficacy for alternative dosing regimens will be addressed by the Division of Reproductive and Urologic Drug Products in their review.

4. The study population contained only 5% (29) of subjects ages 14-16, all from family planning clinics. Although no significant differences in actual use were noticed in this age group as compared to the older group, the small sample size limits conclusions.

5. The small sample size of subjects with less than a completed high school limits conclusions for this population (0.3% with = 8th grade and 13% at 9th -11th grade).

6. Literacy levels of the subjects was not determined.

7. The subjects were allowed to purchase only one package of Plan B (single course of treatment) at a time and had to repeat screening to purchase more. This does not simulate the OTC setting.

8. Follow-up compliance for 2 contacts was 45% as per protocol (5-8 days for the first follow-up and = 28 days for the second follow-up) and 86% in the actual analysis (up to 92 days for the first follow-up and 94 days for the second follow-up) (Table 8). The sponsor did not report the comparability of results between the per-protocol follow-up (45%) and those from the off-protocol follow-up (86%-45% = 41%). The proportion of the off-protocol subjects who returned the Study Data card or had the card in the front of them when the follow-up interview took place was also unknown.

CONCLUSION

1. In excess of 90% of study participants self-selected properly. These results suggest that the correct self-selection rate among OTC consumers would be high.

2. The following limit the generalizability of the study results to an OTC setting:

- The study population was predominantly from family planning clinics
- There was a limited number of enrollees under the age of 16
- Literacy was not determined
- Purchase of Plan B was restricted

- The study was 4 weeks in duration

3. There were no new Plan B safety signals during the 4-week observation period.